

## REMARKS

The foregoing amendments are responsive to the Office Action mailed on May 12, 2006. Claims 1-9 are pending in this application. By election Claims 10 and 11 have been withdrawn from consideration as being drawn to a non-elected invention. Thus, Claims 1-9 are presented for examination.

### Discussion of Amendments to the Specification and Drawings

The Examiner objected to the specification because the disclosure lacked a brief description of the drawings. The specification has been amended to include a brief description of the drawings. Support for the amendment can be found in the specification at pages 5, 6, 9, 10, 14 and 15-19.

### REJECTIONS UNDER 35 USC SECTION 112

The Examiner rejected the claims 1-9 as indefinite under section 112 because claims 1 and 7 recited the limitation “the inner walls” and there is insufficient antecedent basis for this limitation. The Applicants have taken the Examiners suggestion and deleted the word “the” from claims 1 and 7 and replaced it with the phrase “an inner wall”.

The Examiner also rejected claims 6 and 9 as being indefinite because it is unclear what structure is defined by the recitation “Silicon Nitride, a silicon On Insulator (SOI) wafer, and a layer of Silicon Nitride.” It is common knowledge to those well versed in the art of micro-fabrication that the term Silicon on Insulator describes a wafer

type substrate that is composed of a layer of Silicon followed by a layer of Silicon Oxide followed by a layer of Silicon. Accordingly, the recitation in claims 6 and 9 refer to a SOI wafer that is coated on both sides with layers of Silicon Nitride. Nevertheless, the Examiner's point is well taken and the Applicants have amended claims 6 and 9 to make explicit that which is implicit in the term SOI.

#### REJECTIONS UNDER 35 USC SECTION 102

The Examiner rejected claims 1-2 and 7-8 under section 102(b) as being anticipated by Beattie (U.S. Patent No. 5,843,767, issued 1 December 1998). Under §MPEP 706.02, it is well established that for a reference to support a rejection under 35 USC §102, that reference must teach every aspect of the claimed invention. (See also, Verdegaal Bros. V. Union Oil Co. of California, 814 F. 2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.")

The Examiner in citing Beattie states

"[r]egarding claim 1, Beattie teach an apparatus comprising: a substrate having at least one aperture having a tapered portion with a top diameter greater than a bottom diameter and wherein the tapered portion of the aperture transitions into a cylindrical portion having a diameter equal to said bottom diameter of said tapered portion(e.g., Figures 1a and 4...)"

"[r]egarding claim 7, Beattie teach an apparatus comprising: a substrate having at least one aperture having a tapered portion with a top diameter greater than a bottom diameter and wherein the tapered portion of the aperture transitions into a cylindrical

portion having a diameter equal to said bottom diameter of said tapered portion (e. g., Figures 1a and 4)...”

With respect to independent claim 1, while the Examiner is correct in pointing out that Beattie suggests at least one aperture, the Applicants respectfully, disagree that the aperture “transitions into a cylindrical portion having a diameter equal to said bottom diameter of said tapered portion...” as disclosed and claimed by Applicants. For example, Figures 1A and 1B in Beattie show that the apparatus has multiple wells that taper at one end, but they do not taper to a cylindrical portion where the diameter is that of the bottom of the tapered portion. Rather, Figures 1A and 1B show that while the wells in Beattie taper to a cylindrical portion, within the cylindrical portion are a multiplicity of “submicron diameter channels.” Given that there are multiple submicron channels, the diameter of the end of the tapered portion of the wells physically cannot be the same as the diameter of the cylindrical portion of these submicron diameter channels.

By contrast, the Applicants’ apparatus as disclosed in independent claims 1 and 7 teach an aperture where the diameter of the cylindrical portion is the same as the diameter of the end of the tapered portion (see for example, Figure 3 which clearly shows a tapered portion of a single aperture and a cylindrical portion). Beattie, therefore, does not teach each and every element of the invention.

Accordingly, the rejection of independent claims 1 and ,7 and dependent claims, under 102 (b) is improper and should be withdrawn. Applicants’ claims are patentably distinguishable from the apparatus described in Beattie.

The Examiner rejected claim 1, 2, 4, 5, 7 and 8 under section 102(b) as being anticipated by Akeson et al (Biophys. J. Vol. 77, pp.3227-3233 (1999)).

The Examiner is citing Akeson states:

"[r]egarding claim 1, Akeson et al teach an apparatus comprising: a substrate having at least one aperture having a tapered portion with a top diameter greater than a bottom diameter and wherein the tapered portion of the aperture transitions into a cylindrical portion having a diameter equal in diameter to said bottom diameter of said tapered portion (e.g., Figure 1, wherein the cylindrical portion is the part of the figure wherein the lipid bilayer is shown); cross-linkers attached to the inner walls of said aperture (e.g., the lipid bilayer in the aperture; Figure 1); and a macro-cyclic ring, having a diameter substantially the same as the diameter of the cylindrical portion of said aperture, attached at or near the circumference of one end of the cylindrical portion of said aperture (e.g., one  $\alpha$ -hemolysin channel inserted in the bilayer; Figure 1)."

With respect to independent claim 1, Applicants respectfully disagree with the Examiner's characterization of the apparatus described in Akeson. In Akeson the substrate is the lipid bilayer and the Teflon portion of the apparatus is the means by which the lipid bilayer is stretched into a planar surface. The pore, or aperture, in Akeson is not the space between the Teflon supports, but rather the  $\alpha$ -hemolysin protein that is inserted into the lipid bilayer that is stretched between the Teflon supports (see Akeson et. al., at p3227). Accordingly, there is no tapered portion of an aperture, or "channels" as Akeson calls them, only a cylindrical portion, which is what the Examiner calls the  $\alpha$ -hemolysin protein, inserted into the lipid bilayer.

Similarly, there is no macro-cyclic ring described in Akeson. The Examiner identifies the  $\alpha$ -hemolysin protein structure as a macro-cyclic ring. The  $\alpha$ -hemolysin

protein in Akeson, however, is a naturally occurring protein that is isolated from the organism *Staphylococcus aureus*. By contrast a macro-cyclic ring can generally be described as an organic compound, in the organic chemistry sense of the term, containing a large ring, that is, a closed chain of 12 or more carbon atoms; examples include crown ethers, cryptands, spherands, carcerands, cyclodextrins, cyclophanes, and calixarenes. A macro-cyclic ring, as used in the Applicants' invention, is not the same structure as a protein derived from an organism. Furthermore, in Akeson the  $\alpha$ -hemolysin protein is used to create the aperture itself. It is the pore created by the  $\alpha$ -hemolysin protein that creates the channel between the two surfaces. By contrast in the Applicants' invention the aperture structure is created by micro fabrication techniques on a variety of substrates and the macro-cyclic ring is attached to one end of the aperture.

Likewise the Applicants respectfully disagree with the Examiner's characterization of the lipid bilayer in Akeson as a cross linker. As noted above, in Akeson the lipid bi-layer is the substrate within which a channel or pore is created by means of inserting an  $\alpha$ -hemolysin protein. In other words, in Akeson the lipid bi-layer is the substrate, not a cross linker, and the  $\alpha$ -hemolysin protein is the channel or pore. By contrast the Applicants' invention describes cross linkers as "carbon chains" with functional groups designed to bind two molecules together, or to bind a molecule to a surface. (See paragraph 42 of the specification.) In the Applicants invention, cross linkers are used to treat the surface of the aperture so that they are capable of binding biological or chemical anchors such as antibodies and cyclodextrins. (see id.) Cross

linkers in the Applicants invention are not used, and cannot be used, to create the aperture, rather they are used to bind materials to the surface of the aperture.

For these reasons, we respectfully submit, that Akeson does not teach every aspect of the claimed invention as shown in claim 1. Accordingly, Applicants' claims are patentably distinguishable from the structure described in Akeson. Accordingly, the Examiner's rejection of independent claim 1 should be withdrawn. As claims 2, 4 and 5 depend from claim 1 and the Examiner's rejection of claim 1 has been appropriately traversed, the rejections of claims 2, 4 and 5 should likewise be withdrawn.

The Examiner rejected claim 7 for the same reasons as he rejected claim 1. In response, Applicants respectfully makes the same arguments to traverse the Examiner's rejection of claim 1 to traverse the Examiner's rejection of claim 7. Accordingly, the rejection of claim 7 is respectfully requested to be withdrawn. The Examiner also rejected claim 8. As claims 8 depends from claim 7 and the Examiner's rejection of claim 7 has been appropriately traversed, the rejection of claim 8 should likewise be withdrawn.

#### REJECTIONS UNDER 35 USC SECTION 102(a, e)

The Examiner rejected Claims 1-5 and 7-8 under 35 USC 102(a, e) as being anticipated by Letant et al (U. S. Patent application Publication No. US 2002/0191884 A1, published 19 December 2002). The Examiner stated that “[t]he applied reference has

a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e).”

As noted above, “[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” Verdegaal Bros. V. Union Oil Co. of California, 814 F. 2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Accordingly, anticipation will not be found where the prior art fails to disclose a specific feature of the Applicants invention.

The Examiner states that “[r]egarding claim 1, Letant et al teach an apparatus comprising: a substrate having at least one aperture having a tapered portion with a top diameter greater [sic] than a bottom diameter and wherein the tapered portion of the aperture transitions into a cylindrical portion having a diameter equal to said bottom diameter of said tapered portion (e.g., pyramidal nucleation pits are prepared on wafer, followed by pore generation on each pyramid; paragraphs 0035-0037).”

The Applicants respectfully disagrees with the Examiner’s characterization of the nucleation pits in Letant et al as being an aperture with a tapered portion with a top diameter greater than a bottom diameter. The nucleation pits in Letant et al are the starting point from which a pore or aperture is formed in the substrate: “each inverted pyramid will correspond to a pore.” (Letant et al paragraph 35). There is no disclosure of an aperture with a tapered portion that transitions into a cylindrical portion having a diameter equal to said bottom diameter of said tapered portion. To the contrary, Figure 4

in Letant et al clearly shows a resultant aperture pore that has a uniform diameter and is, therefore, cylindrical throughout its length. Figure 4 clearly shows that the aperture in Letant et al does not have a tapered portion.

Similarly, while Letant et discloses a macrocyclic ring (see Figure 3b) these macrocyclic rings are attached entirely within the pore walls (see Figure 4). By contrast the macrocyclic rings in the Applicants invention is substantially the same diameter as the cylindrical portion of the aperture and is attached at or near the circumference of one end of the aperture.

For these reasons, we respectfully submit, that Letant et al does not teach every aspect of claim 1 of Applicants' invention and, therefore, the Examiner's rejection under 102 (a, e) should be withdrawn. Accordingly, Applicants claims are patentably distinguishable from the structure described in Letant et al. As claims 2, 3, 4 and 5 depend from claim 1 and the Examiner's rejection of claim 1 has been appropriately traversed, the rejection of claims 2, 3, 4 and 5 under 102 (a, e) should likewise be withdrawn.

The Examiner rejected claims 7 for the same reasons as he rejected claim 1. In response, Applicants respectfully make the same arguments to traverse the Examiner's rejection of claim 1 to traverse the Examiner's rejection of claim 7. As claims 8 depends from claim 7 and the Examiner's rejection of claim 7 have been appropriately traversed, claim 8 should likewise be allowed.

## REJECTIONS UNDER 35 USC SECTION 103

The Examiner rejected claim 3 "under 35 U.S.C. 103(a) as being unpatentable over Beattie (U.S. Patent No. 5,843,767 issued 1 December 1998) in view of Akeson et al (Biophys. J. vol. 77, pp..3227-3233 (1999) as applied to claim 1 above, and further in view of Hoger (J. Polymer Sci. Part A; Poly Chem., vol. 37, pp.2685-2698 (1999)). Regarding claim 3, the apparatus of claim 1 is discussed above. Neither Beattie nor Akeson et al teach rigid phenylethynyl backbone. However, Hoger et al teach macrocyclic rings comprising rigid phenylethynyl backbones (Abstract) with the added benefit that they host molecules that recognize guest molecules by precise complementarity (page 2687, column 2, lines 19-25)."

Under MPEP §2142, there are three requirements to establish a *prima facie* case of obviousness.

- 1) There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings.
- 2) There must be a reasonable expectation of success.
- 3) The prior art reference (or references when combined) must teach or suggest all the claim limitations.

Applicants respectfully submit that the Examiner has failed to demonstrate a *prima facie* case of obviousness. Under prong three of the test, the prior art references, or

references when combined, must teach or suggest all the claim limitations. Claim 3 depends from claim 1 and thus includes all the limitations of claim 1. Thus, since none of the references either in combination or alone suggest or disclose an apparatus with all the limitations found in Applicants' invention in claim 1, the Examiner's rejection under 103 (a) is inappropriate. For example, neither Beattie nor Akeson et al teach an aperture with a tapered portion and a cylindrical portion as discussed above. Thus, combining these two references would not result in an apparatus as disclosed by Applicants. Similarly, Hoger et al does not teach an aperture with a tapered portion and a cylindrical portion. Accordingly, combining Hoger with Beattie and Akeson results in an apparatus that does not teach or suggest all the limitations of the Applicants invention.

Furthermore, the Examiner characterizes the macrocyclic ring in Hoger as capable of hosting "molecules that recognize guest molecules by precise complementarity." While it may be true that the macrocyclic ring as disclosed in Hoger may be able to host molecules because of chemical complementarity, but that is not what is disclosed in Applicants invention. In the Applicants invention, the macrocyclic ring is anchored at one end of an aperture and to the macrocyclic ring is attached a biological or chemical probe or antibody. It is to this biological or chemical probe or antibody that a target will attach by means of complementarity. Hoger et al does not disclose the use of a biological or chemical probe or antibody. Thus, combining all of the cited references fails to yield the apparatus as disclosed by Applicants. Accordingly, the third prong of the obviousness test has not been met.

Similarly, the first prong of the obviousness test is not met here because there is no suggestion or motivation in the prior art to combine the cited references:

“[o]bviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art.” *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Beattie teaches the use of tapered wells and within each well, multiple cylindrical apertures in a substrate. Akeson et al discloses the use of an  $\alpha$ -hemolysin protein as an aperture in a lipid bilayer.

Applicants respectfully suggests that one of ordinary skill in the art would not find a motivation in the references to properly combine the teachings of these references with that of Hoger to create the apparatus disclosed in claim 3 of Applicants invention. Additionally, there must be a basis in the art for combining or modifying the references to arrive at Applicants' claimed invention. Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination. ACS Hospital Systems, Inc. v. Montefiore Hospital, 221 USPQ 929, 933 (Fed. Cir. 1984) and In re Geiger, 2 USPQ2d at 1278 (Fed. Cir. 1987). There is nothing in any of the cited references to teach, suggest or provide incentive in support of the combination of elements recited in Applicants claim 3.

Additionally, Applicants submit that the first prong of the obviousness test has not been met because any suggestion that the references be combined can only be based on impermissible hindsight. MPEP §2142 states “the tendency to resort to ‘hindsight’ based upon Applicants’ disclosure is often difficult to avoid due to the very nature of the

examination process. However, impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art.” Also, under MPEP §2143.01, “[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination.” *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). As the cited references do not suggest in any way that they should be combined, only through impermissible hindsight is there any rational for combining the references.

Finally, the Examiner has not shown that there would have been a reasonable likelihood of success from combining the structures disclosed in the references. The Examiner simply states that there would have been a reasonable likelihood of success, but there are no facts presented to suggest that this is true. Even if we accept for arguments sake that “[t]he ordinary artisan would have been motivated to make such a modification because such modification would have resulted in host molecules that recognize guest molecules by precise complementarity”, as discussed above, this would not result in the structure disclosed by Applicants.

The Examiner also rejected claims 1, 6, 7 and 9 “under 35 U.S.C. 103 (a) as being unpatentable over Beattie (U.S. Patent No. 5,843,767 issued 1 December 1998) in view of Letant et al (Nature Materials, vol. 2 pp. 391-395 (June, 2003)). Regarding claims 6 and 9, the apparatus of claims 1 and 7 are discussed above. Beattie also teaches the apparatus of claim 7 comprising a substrate having at least one aperture having a tapered portion with a top diameter greater [sic] than a bottom diameter and wherein the

tapered portion of the aperture transitions into a cylindrical portion having a diameter equal to said bottom diameter of said tapered portion....”

Regarding independent claims 1 and 7, neither Beattie nor Letant et al teach an aperture with a tapered portion that transitions into a cylindrical portion as shown in Applicants' independent claims 1 and 7. Rather, Beattie teaches an apparatus where the tapered well transitions into a cylindrical portion wherein there are multiple cylindrical pores. Similarly, Letant et al teaches only a cylindrical pore. Accordingly, the cited references neither disclose nor suggest apertures where there is a tapered portion with a top diameter greater than the bottom diameter and wherein the tapered portion of the aperture transitions into a cylindrical portion having a diameter equal to said bottom diameter of said tapered portion. Thus, even when Beattie is combined with Letant et al, the apparatus that is thus disclosed and claimed is not the apparatus that is disclosed in the Applicants invention in claims 1 and 7. Thus, the third prong of the obviousness test is not met.

For these reasons, Applicants believe they have overcome any rejections of claims 1 and 7 and dependent claims thereof as improper under 103 (a) and is respectfully requested to be withdrawn.

#### Double Patenting

The Examiner provisionally rejected claims 1-9 “on the ground of non-statutory obviousness type double patenting as being unpatentable over claims 1-8, 10-11, 14-15,

17-41, 44-48, and 74-82 of copending Application No. 11/140,391.” Similarly, the Examiner rejected claims 1-9 “on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,785,432 B1 in view of Akeson et al (Biophys. J. Vol. 77, pp. 3227-3233 (1999)).”

Regarding claims **1-9**, in an offer of compromise to expedite the prosecution of the application, the Applicants have enclosed a TERMINAL DISCLAIMER disclaiming the terminal months of any patent granted on the subject application beyond the expiration date of the Letant et al reference, U. S. Patent Application No. 11/140,391. Letant et al. (U. S. Patent Application No. 11/140,391) is assigned to The Regents of the University of California, which is the same assignee as in the present application. Similarly, the Applicants have enclosed a TERMINAL DISCLAIMER disclaiming the terminal months of any patent granted on the subject application beyond the expiration date of the Letant et al reference U.S. Patent No 6,785,432 B1. Letant et al (U.S. Patent No 6,785,432 B1) ) is assigned to The Regents of the University of California, which is the same assignee as in the present application.

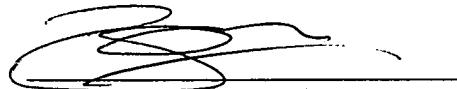
In light of the filing of Terminal Disclaimers, and the appropriate fee, the issue of a nonstatutory double patenting rejection with respect to claims **1-9** is rendered moot.

Summary

Having amended the claims, as discussed above, Applicants respectfully submit that Claims 1 through 9 are in condition for allowance, and Applicants respectfully request allowance of Claims 1 through 9.

In the event that the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, he is respectfully requested to initiate the same with the undersigned at (925) 422-7073.

Respectfully submitted,



John H. Lee

Attorney for Applicants

Registration No. 53,193

Dated: November 15, 2006